4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-N-3976]

Support for Clinical Trials Advancing Rare Disease Therapeutics Pilot Program; Program Announcement

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration's (FDA or Agency) Center for Biologics Evaluation and Research's (CBER) Office of Therapeutic Products (OTP) and Center for Drug Evaluation and Research's (CDER) Office of New Drugs are announcing the opportunity for a limited number of development programs to participate in the Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot Program, with the goal of further accelerating the pace of development of certain CBER- and CDER- regulated products (novel drug and biological products) that are intended to treat a rare disease. Because each Center has identified specific needs concerning regulated products for rare diseases, the eligibility criteria for the pilot differ between CBER and CDER. This pilot would augment the currently available formal meetings between FDA and sponsors by addressing issues related to the development of individual products through more rapid, ad-hoc communication mechanisms. Sponsors, if selected for the pilot, would receive more frequent advice related to such specific issues through additional interactions to facilitate novel drug and biological product program development and generate high quality and reliable data intended to support a Biologics License Application (BLA) or New Drug Application (NDA). This notice outlines the eligibility criteria, what to submit in a request to participate in the pilot, selection criteria, process, and FDA-Sponsor interactions expected to occur for programs participating in the pilot.

DATES: From January 2, 2024, to March 1, 2024, FDA will accept requests to participate in the START Pilot Program and select no more than three participants from each Center (CBER and CDER). See the "Participation" section for eligibility criteria, instructions on how to submit a request to participate, and information regarding the selection process.

FOR FURTHER INFORMATION CONTACT: Andrew Harvan, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7268, Silver Spring, MD 20993-0002, 240-402-7911; or Quyen Tran, Center for Drugs Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6301, Silver Spring, MD 20993-0002, 301-796-2771.

For general questions about the START Pilot Program for CBER: Industry.biologics@fda.hhs.gov. *For general questions about the START Pilot Program for CDER:* CDER.STARTProgram@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

The purpose of the START Pilot Program is to further accelerate the pace of development of novel drug and biological products that are intended to address an unmet medical need as a treatment for a rare disease. The pilot is designed to be milestone-driven (i.e., to facilitate the progression of a development program to pivotal clinical study stage or the pre-BLA or pre-NDA meeting stage) where product development programs selected would benefit from enhanced communications with FDA. Participation in the pilot will be considered concluded when the development program has reached a significant regulatory milestone such as initiation of the pivotal clinical study stage or the pre-BLA or pre-NDA meeting stage as agreed upon with the sponsor. Pilot participants will be selected based on demonstrated development program readiness. The START Pilot Program is intended to provide a mechanism for addressing clinical development issues that otherwise would delay or prevent a promising novel drug or biological product from progressing to the pivotal clinical trial stage or pre-BLA/pre-NDA meeting stage.

The pilot would augment the currently available formal meetings between FDA and sponsors (see FDA's draft guidance for industry entitled "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" ((September 2023) (Ref. 1))) through more rapid, ad-hoc communications with FDA by addressing issues with specific programmatic needs for individual products. For example, these issues can be related to clinical study design, choice of control group, fine-tuning the choice of patient population, selecting appropriate endpoints for efficacy trials to support marketing approval, selecting statistical methodology, leveraging nonclinical information, or product characterization. For eligible development programs sponsors and FDA could benefit from such additional communication beyond the currently available formal meeting mechanisms to address specific programmatic needs that require in-depth discussions. The increased communication between FDA review staff and sponsors is intended to facilitate program development for specific products and to help generate high quality and reliable data intended to support a BLA or NDA.

II. Participation

From January 2, 2024, to March 1, 2024, FDA will accept requests to participate in the START Pilot Program and will initially select up to three participants in each Center. Taking into consideration lessons and sponsors' experiences from the initial iteration of this program, a second iteration of the pilot may be conducted to include more participants in the future. At a later date, FDA may also publish another notice in the *Federal Register* to announce a second iteration of the program.

Sponsors who are interested in participating in the START Pilot Program should submit a request to participate as an amendment to their Investigational New Drug (IND) application.

A. Eligibility Criteria

To be considered for the START Pilot Program, participants must meet the following eligibility criteria:

1. Joint CBER and CDER Eligibility Criteria

- IND has been submitted in or converted to Electronic Common Technical Document (eCTD) format, unless the IND is of a type granted a waiver from eCTD format (see FDA's guidance for industry entitled "Providing Regulatory Submissions in Electronic Format--Certain Human Pharmaceutical Product Applications and Related Submissions using the eCTD Specifications" ((February 2020) (Ref. 2))) and remains in active status.
- Sponsor has demonstrated substantial effort to ensure that that Chemistry, Manufacturing, and Controls (CMC) development aligns with clinical development, for example, through documented control of manufacturing and testing procedures to ensure clinical and CMC development timeline are in alignment.

Given the specific identified needs for the products regulated by each Center for rare diseases, the following eligibility criteria differ between CBER and CDER:

2. CBER-Specific Eligibility Criteria
   - Existing OTP-regulated IND for a cellular or gene therapy under which the product is being developed toward a marketing application.
   - Such product is intended to address an unmet medical need as a treatment for a rare disease[1] or serious condition, which is likely to lead to significant disability or death within the first decade of life.
3. CDER-Specific Eligibility Criteria
   - Such product is intended to treat rare neurodegenerative conditions (including those of rare genetic metabolic etiology).

B. What to Submit in a Request to Participate in the START Pilot

[1] A rare disease or condition "means any disease or condition which affects less than 200,000 persons in the United States…" (Section 526(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb(a)(2))). The START Pilot Program in CBER is not intended to encompass all rare diseases, but only a subset of rare diseases that are likely to lead to significant disability or death within the first decade of life.

To participate in the START Pilot Program, sponsors should submit a written request as an amendment to the IND. The cover letter should (1) state "Request to participate in the START Pilot Program", (2) note whether there is a breakthrough therapy (BT) designation for the product and for CBER-regulated products only- whether there is a BT designation and/or regenerative medicine advanced therapy (RMAT) designation, and (3) provide a point of contact.

The request should include the initial specific development issue(s) for a given product for enhanced communication and a proposed communication plan between the sponsor and review staff. In addition, the following information should be provided:

1. Program development plan

The plan should describe the current state of program development, including any ongoing activities not already detailed in the IND.

- CMC development plan and current status.
- Nonclinical development plan and current status.
- Clinical development plan and current status.

2. Any specific issue(s) (grouped by review disciplines) for which the prospective applicants are seeking enhanced communications with FDA review staff to facilitate program development, including, for example, to ensure a mutual understanding of information needed to facilitate initiating the pivotal clinical study or to the pre-BLA/pre-NDA meeting stage.

3. The planned timeline for initiation of the clinical study(ies) intended to provide the primary evidence of effectiveness to support a marketing application or for a pre-BLA/pre-NDA meeting request.

4. The proposed communication plan for interactions between FDA review staff and the sponsor, including the proposed timing (i.e., month and year) for the initial teleconference and format (e.g., email or teleconference) of the subsequent communications on a scheduled and/or as needed basis.

C. Selection Criteria and Process

FDA intends to select participant CBER and CDER INDs based on the criteria outlined below. FDA will make its determination of participants following the close of the application period. FDA intends to issue a letter to notify each sponsor of FDA's decision on sponsor requests to participate within 90 days of the application deadline.

For the initial selection of up to three INDs from each Center for the START Pilot Program from eligible applicants, FDA intends to consider factors such as: (1) potential clinical benefits of the product, (2) whether resolution of the specific issues noted by the sponsor in their request to participate in the pilot could be facilitated through enhanced communication to improve efficiency of program development, (3) whether there is an BT or RMAT designation for the product, (4) whether CMC development timeline aligns with clinical development plans, and (5) while INDs for combination products (21 CFR 3.2(e)(1)) may be eligible, products that require significant cross-Center interactions (e.g., complex combination products) may be less likely to be selected for the pilot. Overall, pilot participants will be selected based on application readiness (e.g., sponsors who demonstrate having the ability to move the program forward towards a marketing application).

D. FDA-Sponsor Interactions During the START Pilot Program

If selected for the START Pilot Program, sponsors will receive enhanced communications with FDA review staff. These enhanced communications may vary between CBER and CDER but will include at a minimum an initial meeting to review features of the pilot, discuss a pathway intended to support a marketing application, and to discuss specific issues for which a sponsor requests enhanced communication with FDA. Additional communications will include ongoing interactions via email or teleconference that take place on a scheduled and/or as needed basis as agreed upon by the sponsor and FDA.

III. Paperwork Reduction Act of 1995

This notice refers to previously approved FDA collections of information. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014 and the collections of information in 21 CFR part 601 have been approved under OMB control number 0910-0338.

IV. References

The following references are on display at the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500, and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at https://www.regulations.gov. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. FDA Draft Guidance for Industry "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" (September 2023): https://www.fda.gov/media/172311/download.
2. FDA Guidance for Industry "Providing Regulatory Submissions in Electronic Format--Certain Human Pharmaceutical Product Applications and Related Submissions using the eCTD Specifications" (February 2020): https://www.fda.gov/media/135373/download.

Dated: September 25, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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